

IN THE SPECIFICATION:

a. On page 15, replace the first paragraph, lines 3-6, with:

--Figs. 1A through 1D ~~shows~~ show the enrichment of TIL-B phage displayed Fab libraries for binding of breast cancer cell surface antigens. Libraries were enriched by six sequential rounds of panning and regrowth of cell binding phage. The library derived from patient 14 was panned on MCF7 cells. The patient 16 library was panned on the breast cancer cell lines SKBR3, MCF7, and 2087.--

b. On page 15, replace the second paragraph, lines 8-13, with:

--Figs. 2A through 2H ~~shows~~ show the flow cytometry analysis of phage Fab libraries and individual Fab clones. Libraries 14.6 and 16.6 are shown after enrichment for breast cancer cell binding; individual Fab clones 14.6.11, 14.6.19 (SEQ ID NO: 1; SEQ ID NO: 3), 14.6.20 (SEQ ID NO: 2; SEQ ID NO: 4), and 16.4.19) are also shown. Patient 14 library was panned on MCF7 cells; Patient 16 library was panned on MCF7, SKBR3, and 2087 breast cancer cells. Only data from SKBR3 panning is shown.--

c. On page 16, replace the third full paragraph, lines 13-18, with:

--Figs. 7A and 7B shows show a summary of TILB marker expression. ~~Upper table FIG. 7B~~ indicates FACS results (~~underneath table~~); ~~lower left table~~, while FIG 7A indicates results of TILB immunohistochemistry. Numbers in ~~upper table FIG. 7B~~ indicate percentage of cells that are positive for the first antigen which are also positive for the second antigen. For example, 95% of CD19+ TIL are also IgG+. These preliminary numbers are based on averages, and have not yet been subjected to statistical analyses.

d. On page 22, replace the first paragraph, lines 2-16, with:

--To determine if TIL-B immunoglobulins were reactive with tumor, 2 phage-displayed immunoglobulin Fab libraries were generated from geriatric patient TILs by the methods of Barbas et al (Barbas, C.F. 2000. Phage display: a laboratory manual. Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY). Fab (heavy chain variable region plus CH1 and light chain) libraries of  $\sim 1 \times 10^7$  Fab clones were cloned in the pCOMBX phage display vector (gift of C. Barbas, Scripps Research Institute, San Diego, CA). The inventor Julia Coronella received training in phage display from Dr. Carlos Barbas of Scripps Research Institute at the Cold Spring Harbor course on phage display 2000. The libraries were panned on cultured breast cancer cells in order to enrich for Fabs that bind breast cancer cell surface antigens. Panning consisted of 6 sequential rounds of incubation of phage displayed Fabs with breast tumor cells under increasingly stringent conditions to isolate high affinity Fabs, and regrowth of the binding fraction. Enrichment of patient 14 Fab library for tumor cell binding was observed after 4 sequential rounds of panning on MCF7 cells (Figure 1). Enrichment of patient 16 Fab library for

tumor cell binding was observed after only 1 panning on SKBR3, MCF7 and 2087 breast cancer cells, indicating a high fraction of tumor binding Fabs in the library (Figs. 1A through 1D).--

e. On page 23, replace the last paragraph, lines 14-21, with:

--Thus far, 3 Fabs with apparent specificity for breast tumor cells have been isolated from the patient 14 Fab library (Figs. 2A-2H). Fab 14.6.11 binds all breast cancer cell lines tested but not nonmalignant healthy breast epithelium, primary fibroblasts or the leukemia cell line HL60. Fabs 14.6.19 (SEQ ID NO: 1; SEQ ID NO: 3) and 14.6.20 (SEQ ID NO: 2, SEQ ID NO: 4) were also highly specific for breast cancer, but less universal binding of breast cancer cell lines was observed. A number of promising Fabs were isolated from the patient 16 library and are currently under analysis. Monovalent phage Fabs have low avidity, and the FACS protocol utilized is a lengthy multi-step staining. Therefore, Fab clones--

f. On page 28, replace the first paragraph, lines 1-17, with:

--cells. Six breast tumors, 5 tumor-draining lymph nodes, peripheral blood from 5 breast cancer patients, and peripheral blood from 4 healthy donors were analyzed. Data is summarized in Figs. 7A and 7B. As occurs in a lymph node follicle, the populations of TILB were heterogeneous. Most TILB were IgG+, IgM-, and approximately half were IgD+. All TILB were CD5-. Some B cells expressed low levels of CD38, as do centroblasts and centrocytes. However, no CD38hi cells were observed, consistent with the lack of plasma cells determined by

immunohistochemistry. The absence of plasma cells can be explained by apoptosis or alternatively, by a deficit in the plasma cell differentiation pathway. Centroblasts and centrocytes are normally CD95+, and very sensitive to apoptosis. In contrast, most TILB express CD40, but not CD95 (Fas). Strong BCL2 expression of TILB was determined by immunohistochemistry, and is unusual in that only plasma cells and germinal center founder cells normally express this antiapoptotic protein. BCL2 expression protects germinal center B cells from apoptosis in vivo. Through expression of the antiapoptotic proteins CD40 and BCL2, and lack of CD95 expression, TILB may be unusually resistant to apoptosis. Resistance to apoptosis is consistent with the inventor's demonstration of autoreactive antibodies from TILB, as autoreactive B cells are normally deleted during the germinal center reaction. One can speculate that cytokines from local activated T lymphocytes or perhaps cytokine secretion from the tumor itself may induce this antiapoptotic profile.--